One should not lose sight of the scale of the problem. We only found two cases in 1758 biopsy specimens where the diagnosis of papillary carcinoma led to resection of a papillary microcarcinoma as well as the benign nodule which was the palpable lesion. Any procedure that increases the chance of finding a clinically insignificant microcarcinoma, such as multiple blind biopsies of non-nodular thyroid tissue or of ultrasound detected lesions of less than 1 cm in diameter, should be very carefully evaluated before being introduced into routine use.¹ Multiple blind needle biopsies obviously increase the chance of detecting clinically insignificant lesions—papillary microcarcinomas may occur in as many as 34% of adult thyroids when they are histologically examined in 2 to 3 mm steps. If those thyroids were thoroughly examined histologically, it was estimated that about 300 microcarcinomas would have been found.² The prevalence of thyroid cancer will increase still further with an increasing number of sections studied per gland.³ Not to mention primary thyroid lesions where fine needle aspiration cytology, serum calcitonin levels or genetic studies helped to yield a diagnosis of an unsuspected medullary microcarcinoma where thyroidectomy should be advocated.⁴

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Leukaemia immunophenotyping: effect of antibody source and fluorochrome on antigen detection

We read with interest the recent publication by Howard *et al*¹ in which the authors highlight discrepant findings of myeloid antigen expression in cases of childhood acute lymphoblastic leukaemia (ALL). They concluded that the detection of antigens CD13 and/or CD33 may be dependent upon both the commercial source of antibody and the type of fluorochrome used. We wish to add support to their conclusions by reporting results from the United Kingdom National External Quality Assurance Scheme (UK NEQAS) for leucocyte immunophenotyping, in addition to data from our own investigations.

Results from UK NEQAS surveys have frequently shown variability in antigen detection attributable, in part, to the use of different commercial monoclonal antibodies. In survey 935, for example (acute biphenotypic leukaemia), the following mean values for CD13 expression were obtained for each reagent: Becton Dickinson (LeuM7) 15% (n=15), Dako 13.2% (n=27), Coulter 48.25% (n=8), Seralab 3% (n=2), Ortho 0.5% (n=2), and Serotec 89% (n=1). In addition, the scheme has consistently shown statistically significant differences between samples analysed with fluorescein isothiocyanate (FITC) and phycoerythrin (PE) conjugated antibodies for the following antigens: CD3, CD5, CD13, CD14, CD19, and CD33. In survey 923, investigating CD13 detection in a case of acute myeloid leukaemia, eight of 24 laboratories using FITC conjugated antibodies obtained values less than 50% (overall mean 58%), of which three were negative results, as defined as less than 20%.² In contrast, all 12 laboratories using PE conjugated antibodies obtained results greater than 50% (mean 77%). This variation may be as a result of PE having a higher quantum yield than FITC, thus potentially increasing sensitivity.

In a parallel study to that of Howard and colleagues¹ we have recently determined the expression of myeloid antigens in B cell chronic lymphocytic leukaemia (B-CLL). As with childhood ALL such "aberrant myeloid" expression has been reported to be of prognostic significance.² To confirm these findings we examined 53 cases of B-CLL (stages 0 to IV), using Becton Dickinson PE conjugated anti-CD13 and anti-CD33 (clones L138 and P67.6, respectively), by whole blood lysis and triple colour staining. In 51 cases fewer than 4% of B cells expressed either CD13 or CD33 (6% in two cases) when compared with isotype matched controls. Mean fluorescence staining intensity (MFSI) for both CD13 and CD33 expression did not differ significantly from the negative controls. Previous studies, reporting positive myeloid antigen expression, predominantly used Coulter anti-CD13 (MY7) and anti-CD33 (MY9) thus raising the possibility that these discrepant findings may relate to antibody source. To confirm this hypothesis we re-examined 15 of the B-CLL cases with PE conjugated MY7 (CD13) and MY9 (CD33). Of these, nine expressed the CD33 antigen on $\geq 10\%$ of the leukaemic B cells, with five cases being regarded as positive ($>20\%$ expression); results in agreement with previous studies. The MFSI values showed a significant increase when compared with controls ($p<0.001$). No sample expressed CD13 on $>20\%$ of the leukaemic B cells (one had 12%) although the values were significantly raised when compared with those obtained using Becton Dickinson antibodies ($p<0.001$). We feel, therefore, that antibody source and also the fluorochrome used should be taken into account when comparing reports studying "aberrant" myeloid antigen expression.

Data from UK NEQAS, together with our own studies in B-CLL, support the conclusions of Howard and colleagues and raises several important issues. Firstly, which result is right? This question may only be answered if all commercially available reagents are standardised; an important consideration when collecting immunophenotypic data in multicentre trials, particularly if meaningful diagnostic and prognostic information is to be obtained. Secondly the development of newer and more sensitive fluorochromes, coupled with multiparameter technology, will increase the dilemma as to what should be regarded as positive. The simplistic approach using an arbitrary cut off point, as suggested

in the recent BSCH guidelines,³ will probably not be applicable in the future. Data analysis procedures which currently employ the placement of a cursor at the boundary of the negative population are likely to be inappropriate. More biologically relevant procedures, such as antigen density quantification using calibrated flow cytometers, may yield more meaningful data.⁴ Finally, despite the experience of a number of quality control schemes worldwide, there is no consensus as to the best antibody within a CD group for diagnostic use. Such evaluations would require the production of reference materials which express the antigens of clinical importance. Research in this area is currently under way,⁵ although the technical difficulties must not be underestimated.

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Recurrent thrombotic occlusions of arteries and veins caused by intravascular metastatic adenocarcinoma

I refer to the case reported by Levi *et al*¹ of a young woman with recurrent vascular occlusions found at necropsy to be caused by microscopic metastatic adenocarcinoma. They rightly suspected the presence of malignant disease during life, but despite wide-ranging invasive, radiological and laboratory investigations were unable to confirm their clinical suspicion. In their last sentence, the authors speculate that cytological examination of the blood, using specific markers for malignant cells, might have detected the adenocarcinoma cells; this may have been so, but I wonder if they performed bone marrow trephine biopsy as it is not mentioned amongst the many investigations listed in their paper. Similarly, no mention was made of bone marrow studies carried out on post-mortem tissues.

It is thought that one large trephine biopsy or bilateral biopsies can provide a detection rate of metastatic disease somewhere in the region of 60%. Certainly, it is a worthwhile investigation in the type of case reported by Levi *et al* and if performed might have resulted

in establishing the cause of the patient's recurrent thrombotic occlusions in life.

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Dr Levi comments:

Although not reported in our paper, a bone marrow trephine biopsy was performed in our patient and did not reveal any abnormalities. At necropsy, however, bone marrow studies were not carried out and therefore malignant cells may have been missed in the original biopsy. We can only underline the importance of bone marrow studies in patients with suspected but unconfirmed malignant disease.

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A proposed SI unit for number

I believe that a dimensionless unit for number (unit) would be valuable, fill a gap, simplify the expression of very large and very small numbers, and in pathology have particular use for particle counts. I propose the "quant", a name which suggests its use and is linguistically neutral, and the symbol "q", following the convention that only units named after a scientist use an upper case letter in their symbol — except for L as the alternative to l for the litre. The quant would carry the standard prefixes for multiples and sub-multiples used with all symbols for units.¹ For example, an erythrocyte count in health, instead of 5.1×10^{12} , which requires a multiplication sign and a superscript and can be inconvenient for typing and word-processing, would be 5.1 Tq/l (teraquants per litre) and similarly a leucocyte count would be 6.8 Gq/l.

Perhaps such a unit has already been considered and rejected by the International Committee for Weights and Measures (CIPM)?

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Urea and ammonium concentrations in serum and gastric juice in children with and without *H pylori* infection. Results presented as means and ranges

<i>H pylori</i> status	Blood serum		Gastric juice	
	Urea (mmol/l)	Ammonium (mmol/l)	Urea (mmol/l)	Ammonium (mmol/l)
Positive	4.12 ± 0.46 (2.2-7.5)	0.04 ± 0.01 (0.03-0.05)	1.37 ± 0.14 (0.09-3.33)	2.79 ± 0.44 (0.68-3.34)
Negative	4.46 ± 0.41 (2.3-7.8)	0.04 ± 0.02 (0.02-0.06)	3.56 ± 0.36 (1.04-5.36)	0.27 ± 0.09 (0.0331-0.69)

Intragastric urea hydrolysis in children infected with *Helicobacter pylori*

We read with interest the article by Neithercut *et al*¹ reporting the measurement of urea and ammonium concentrations in gastric juice in patients infected with *Helicobacter pylori*. This research is important as this non-invasive technique may be of diagnostic value, particularly in children, and also because diagnosis of *H pylori* infection following biopsy of the gastric mucosa may lead to false negative results due to patchy dissemination of the organism.²

Here, we report the measurement of urea and ammonium concentrations in gastric juice in 63 children (mean age 9.4 ± 2.3 years, range 5 to 14 years) with *H pylori* associated gastritis. The control group comprised 24 children in the same age range with *H pylori* infection. *H pylori* infection was diagnosed by the rapid urease test, histological examination following staining with Giemsa and serological analysis for the detection of specific IgG antibodies (Roche, Switzerland).³ Urea and ammonium concentrations in gastric juice and blood serum were measured using a manual diacetylmonoxime method (Lachema, Brno, Czechoslovakia) and a modified Keller⁴ method, respectively. Gastric juice pH was also measured. Children with bile reflux were excluded from this study to reduce the possibility of false positive results.⁵ Statistical analysis was performed using the parametric Student's *t* test.

The results of our study are summarised in the table. The results showed significant differences between the urea and ammonium concentrations in gastric juice of children with and without *H pylori* infection ($p < 0.01$).

The concentrations of these substrates in blood did not exceed normal values and did not differ significantly from each other ($p > 0.05$), therefore, serum concentrations cannot influence the concentrations of those substrates in gastric juice.

Statistical analysis suggests that the pH of gastric juice does not correlate with urea and ammonium concentrations and that the urea and ammonium concentrations do not correlate with each other.

In conclusion, measurement of urea and ammonium concentrations in gastric juice may be useful for the diagnosis of *H pylori* infection in children.

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